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| 10/560,650 | 05/09/2006 | David B. Weiner | UPAP0020-100 | 2255 |

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Pepper Hamilton LLP
400 Berwyn Park
899 Cassatt Road
Berwyn, PA 19312-1183

| EXAMINER | |
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| SHEN, WU CHENG WINSTON | |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| **Advisory Action Before the Filing of an Appeal Brief** | **Application No.** 10/560,650 | **Applicant(s)** WEINER ET AL. | |
|---|---|---|---|
| | **Examiner** WU-CHENG Winston SHEN | **Art Unit** 1632 | |

***--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --***

THE REPLY FILED 22 March 2010 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1,14-17,19,55-60,66-71 and 77*.
   Claim(s) withdrawn from consideration: *38,64 and 75*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

Continuation of 5. Applicant's reply has overcome the following rejection(s):

(I) Applicant's claim amendments filed on 03/22/2010 have overcome the rejection of claim 77 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, because the claim has been amended.

(II) Applicant's claim amendments filed on 03/22/2010 have overcome the scope of enablement rejection of claims 21-23, 54, 61-63, 65, 72-74, and 76 under 35 U.S.C. 112, first paragraph, because these claims have been cancelled.

Continuation of 11. does NOT place the application in condition for allowance because:

(I) Applicants request that the finality of the rejection be reconsidered and withdrawn. Applicant argues that the rejection as applied to claim 1 could have been applied to claim 1 prior to the amendment, and the amendment did not necessitate the new grounds for rejection. The rejected subject matter was included in claim 1 prior to the amendment and the rejection as currently applied could have been made earlier.

In response, Applicant apparently fails to understand, intentionally or unintentionally, the inclusion of claim 1 in the 103 rejection of claim 77 is due to the fact that claim 77 is dependent from claim 1. This is the standard format how a 103 rejection is constructed when there is only one 103 rejection or when the first 103 is formatted as "A in view of B" along with additional 103 rejections formatted as "A in view of B, and further in view of C". In this case, there is only one 103 rejection in the Final office action mailed on 01/22/2010, and claim 77 was filed AFTER the Non-Final office action mailed on 07/29/2008. Therefore, there is no double whatsoever that the rejection of claims 1 and 77 under 35 U.S.C. 103(a) as being unpatentable over Yang et al. (Yang et al., Induction of potent Th1-type immune responses from a novel DNA vaccine for West Nile virus New York isolate (WNV-NY1999). J Infect Dis. 184(7):809-16, 2001) in view Letvin et al. (WO 99/16466, international publication date 04/08/1999), is NECESSITATED BY CLAIM AMENDMENTS FILED ON 01/29/2009. Furthermore, Applicant is reminded that claim 1 REMAINS rejected under multiple 102 rejections.

(II) Applicant's arguments have failed to overcome the rejection of claim 66 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant's arguments filed 03/22/2010 have been fully considered and they are not persuasive. Previous rejection is maintained for the reasons of record advanced on page 4 of the office action mailed on 01/22/2010.

Applicant argues that the limitation of non-IgE protein in claim 66 applies to the non-IgE protein in claim 1. While claim 1 itself includes two alternative limitations, i.e. a non-IgE protein from the same species as the IgE signal peptide or a non-IgE protein that is one of several expressly recited immunomodulatory proteins, the additional limitation in claim 66 is clear in indicating that the non-IgE protein that is from the same species as the IgE signal peptide is an immunomodulatory protein or the non-IgE protein is one of several expressly recited immunomodulatory proteins without limitation to whether or not it is from the same species. Therefore, Applicant asserts that claim 66 is clear and definite.

In response, claim 66 depends from claim 1 and recites the limitation "wherein the non-IgE protein is an immunomodulating protein". It is unclear "the non-IgE protein" recited in claim 66 is referring to "a non-IgE protein sequences" recited in lines 3-4 of claim 1 or referring to "a non-IgE protein sequences" recited in lines 6-7 of claim 1. In latter scenario, lines 7-8 of claim 1 had been amended to recite additional limitation "wherein the non-IgE protein is an immunomodulating protein selected from the group considting of ---", thereby, claim 66 simultaneously recites two distinct scopes of "a/the non-IgE protein sequences".

(III) Applicant's arguments have failed to overcome the rejection of claims 1, 14-17, 19, 55-60, and 66-71 under 35 U.S.C. 102(a) and 102(e) as being anticipated by Weiner et al. (US 2002/0123099, A1, Publication date Sep. 5, 2002). Applicant's arguments filed 03/22/2010 have been fully considered and they are not persuasive. Previous rejection is maintained for the reasons of record advanced on pages 14-17 of the office action mailed on 01/22/2010.

Applicant argues that the West Nile virus capsid protein taught by Weiner et al. does not anticipate either the limitation (i) "a nucleic acid sequence that encodes a fusion protein that consists of a non-IgE protein sequences linked to an IgE signal peptide that is from the same species as the non-IgE protein" or the limitation (ii) "a nucleic acid sequence that encodes a fusion protein that consists of a non-IgE protein sequences linked to an IgE signal peptide, wherein the non-IgE protein is an immunomodulating protein selected from the group consisting of cytokines, chemokines, cellular death receptors, cellular adhesion molecules, cellular growth factors, cellular growth factor receptors, protein kinases and enzymes or functional fragment thereof" are two different nucleic acids that can be selected from to be the claimed "isolated nucleic acid" recited in claim 1.

In response, the limitation "from the same species as the non-IgE protein" recited in claim 1 certainly encompasses "obtained from the same species as the non-IgE protein". Applicant is reminded that a virus cannot express viral genes outside of host cells and the viral proteins must be synthesized in the host cells and obtained from the host cells. Therefore, the Examiner maintains the position that the West Nile virus capsid protein taught by Weiner et al. DOES anticipate the limitation "a nucleic acid sequence that encodes a fusion protein that consists of a non-IgE protein sequences linked to an IgE signal peptide that is from the same species as the non-IgE protein".

(IV) Applicant's arguments have failed to overcome the rejection of Claims 1, 14, 16, 17, 19, 55, 56, 58-60, 66, 67, and 69-71 under 35 U.S.C. 102(b) as being anticipated by Yang et al. (Yang et al., Induction of potent Th1-type immune responses from a novel DNA vaccine for West Nile virus New York isolate (WNV-NY1999). J Infect Dis. 184(7):809-16, 2001). Applicant's arguments filed 03/22/2010 have

been fully considered and they are not persuasive. Previous rejection is maintained for the reasons of record advanced on pages 17-20 of the office action mailed on 01/22/2010.

Applicant's arguments and Examiner's Response to Applicant's arguments are the same as documented in the maintained rejection of claims 1, 14-17, 19, 55-63, and 66-71 rejected under 35 U.S.C. 102(a) and 102(e) as being anticipated by Weiner et al. (US 2002/0123099, A1, Publication date Sep. 5, 2002).

(V) Applicant's arguments have failed to overcome the rejection of claims 1, 14, 16, 17, 19, 55, 56, 58-60, 66, 67, and 69-71 under 35 U.S.C. 102(b) as being anticipated by Yang et al. (Yang et al., Induction of inflammation by West Nile virus capsid through the caspase-9 apoptotic pathway. Emerg Infect Dis. 8(12):1379-84, 2002). Applicant's arguments filed 03/22/2010 have been fully considered and they are not persuasive. Previous rejection is maintained for the reasons of record advanced on pages 20-22 of the office action mailed on 01/22/2010.

Applicant's arguments and Examiner's Response to Applicant's arguments are the same as documented in the maintained rejection of claims 1, 14-17, 19, 55-60, and 66-71 rejected under 35 U.S.C. 102(a) and 102(e) as being anticipated by Weiner et al. (US 2002/0123099, A1, Publication date Sep. 5, 2002).

(VI) Applicant's arguments have failed to overcome the rejection of claims 1 and 77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang et al. (Yang et al., Induction of potent Th1-type immune responses from a novel DNA vaccine for West Nile virus New York isolate (WNV-NY1999). J Infect Dis. 184(7):809-16, 2001) in view Letvin et al. (WO 99/16466, international publication date 04/08/1999). Applicant's arguments filed 03/22/2010 have been fully considered and they are not persuasive. Previous rejection is maintained for the reasons of record advanced on pages 22-27 of the office action mailed on 01/22/2010.

Applicant argues that to combine Yang 1 and Letvin to produce the claimed invention as suggested in the Office Action, one skilled in the art would insert the IL-15 coding sequences in place of the West Nile Virus capsid protein sequence. The resulting construct however would comprise an IgE signal peptide linked to an IL-15 protein that contains its own signal peptide. One skilled in the art would not produce such a construct because one skilled in the art would not include two signal peptides in view of the combined teachings. Such a construct is not obvious.

In response, as stated in the maintained rejection for the reasons of record advanced on pages 22-27 of the office action mailed on 01/22/2010, it would have been prima facie obvious to one having ordinary skill in the art at the time of the invention to combine the teachings of Yang et al. regarding a recombinant DNA vaccine, a plasmid construct, as a pharmaceutical composition comprises a nucleic acid sequence encoding the human immunoglobulin secretory leader signal (See sIg leader, indicated in Figure 1A, Yang et al., 2001, and the plasmid map provided below) fused West Nile Virus (WNV) capsid protein (Cp), with the teachings of Letvin et al. regarding the use of plasmid-expressed cytokine IL-15 as a strategy for amplifying immune responses elicited by plasmid DNA vaccines, to arrive at claim 77 of instant application by substitution of WNVCp encoding sequences taught by Yang et al. with IL-15 coding sequence and fused to sIg leader in the context of the plasmid taught by either Yang et al. (2001) or Letvin et al. (1999).

One having ordinary skill in the art would have been motivated to combine the teachings of Yang et al. and Letvin et al. because Letvin et al. specifically teaches the expression of cytokines, including IL-15 and IL-2, as a strategy for amplifying immune responses elicited by plasmid DNA vaccines.

Applicant is reminded that claim 77 recites “functional fragment thereof” IL-15. Substitution (or combination) of one signal peptide with another signal peptide to test functionality of a signal peptide (or signal peptides) of interest is certainly a routine optimization for desired expression level, which is well-know to a skilled artisan. In this regard, Applicant’s attention is directed to MPEP 2144.05.

2144.05 [R-5] Obviousness of Ranges

See MPEP § 2131.03 for case law pertaining to rejections based on the anticipation of ranges under 35 U.S.C. 102 and 35 U.S.C. 102/103.

II. OPTIMIZATION OF RANGES
A. Optimization Within Prior Art Conditions or Through Routine Experimentation
Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. “[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.” In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 (“The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.”); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of

the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

B. Only Result-Effective Variables Can Be Optimized

A particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. In re Antonie, 559 F.2d 618, 195 USPQ 6 (CCPA 1977) (The claimed wastewater treatment device had a tank volume to contractor area of 0.12 gal./sq. ft. The prior art did not recognize that treatment capacity is a function of the tank volume to contractor ratio, and therefore the parameter optimized was not recognized in the art to be a result-effective variable.). See also In re Boesch, 617 F.2d 272, 205 USPQ 215 (CCPA 1980) (prior art suggested proportional balancing to achieve desired results in the formation of an alloy).

With regard to asserted requirement for a specific teaching, suggestion, or motivation, the Examiner would like to direct Applicant's attention to recent decision by U.S. Supreme Court in KSR International Co. v. Teleflex, Inc. that forecloses the argument that a specific teaching, suggestion, or motivation is an absolute requirement to support a finding of obviousness. See recent Board decision Ex parte Smith, --USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (available at http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf) (citing KSR, 82 USPQ2d at 1936). The Examiner notes that in the instant case, even in the absence of recent decision by U.S. Supreme Court in KSR International Co. v. Teleflex, Inc., the suggestion and motivation to combine Yang et al. (2001) and Letvin et al. (1999) have been clearly set forth above in this advisory action and in the maintained rejection of the Final office action mailed on 01/22/2010.

It is noted further noted that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

/Wu-Cheng Winston Shen/
Primary Examiner, Art Unit 1632